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Green Tea Modulation of Obesity and Breast Cancer Risk

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14. ABSTRACT
With estimated 232,340 new cases in 2013, breast cancer continues to be the most frequently diagnosed non-skin cancer among American women.[1] It is also predicted that 39,620 women lose their lives as a result of breast cancer in 2013 in the United Sates, which still keeps the breast cancer as the second leading cause of cancer death.[1] Obesity is a known risk factor for breast cancer in postmenopausal women.[2] Green tea consumption has been shown to be related with decreased body weight and it is thought that it may also reduce inflammation.[3-6] The goal of this training grant is to study changes in the obesity and energy-related hormones as well as inflammatory markers in healthy postmenopausal women at high risk of breast cancer due to dense breast tissue who consume green tea supplements containing 800 mg epigallocatechin-3-gallate (EGCG) daily for 12 months. Major milestones of this study include recruiting and randomizing all of the training grant study participants, and completing the study for 90% of the target sample size. It is expected that the last participant completes the study for this training grant by the end of July 2013. Lastly, analyses of all biological samples in serum and plasma will start in early May 2013, and it is anticipated that the last run of analyses to be finished by the middle of August 2013.

15. SUBJECT TERMS
Green tea, Breast cancer risk, Obesity, epigallocatechin-3-gallate (EGCG), energy-related hormones, inflammatory biomarkers, postmenopausal women.

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INTRODUCTION

Green tea intake has been associated with reduced risk of breast cancer, [7] however, mechanisms through which green tea may lead to lower breast cancer risk has not been elucidated yet. Among proposed mechanisms, reduction in body weight and/or body fat mass as well as inflammation has drawn a great deal of attention within the cancer research community.[3-6] This training grant aims at evaluating the effects of green tea extract intake on the circulating levels of the energy and obesity-related hormones and inflammatory biomarkers in healthy postmenopausal women, and whether any observed changes vary by the catechol-O-methyltransferase (COMT) genotype. Abovementioned measurements will be performed from the baseline and 12-month visits of a randomized, double-blind, placebo-controlled prevention trial in a population of overweight and obese participants at high risk of breast cancer due to dense breast tissue.

BODY

There has been a great deal of progress with enrollment for the Green Tea Modulation of Obesity and Breast Cancer Risk study. As of April 4, 2013, study has been completed for 90% of the final sample size. In addition, it is expected that the remaining 10% of the study participants finish this training grant by the end of July 2013. This is in an entire agreement with the proposed timeline schedule for completing the study. Due to slow recruitment rate and lower than expected prevalence of the high activity COMT group, there were previously some concerns with recruitment of enough high activity COMT genotype participants. However, given current enrollment profile, it is anticipated that there will be no problem with completing the trial for this group. Therefore, this clinical trial maintains enough power to explore effect modification by *COMT* genotype.

At this time, the drop-out rate is below 12% which shows we have been successful in retaining participants in the study. Also, compliance to the supplementation regime has been 96.9% that shows study participants comply with the study protocol and guidelines very well.

In terms of the study biological sample analyses, the PI will supervise and run all assays during May 2013 to August 2013 with the help of a skilled lab technician. It had been proposed in the last year annual report that blood sample analyses will start in early April 2012; however, due to issues involved with assays' variability, it has been decided to start sample analyses when all study samples are ready for hormones and biomarkers measurements. Hopefully, this approach will contribute to lower within-batch and between-batch variability data.

On the other hand, the data cleaning part of the study has already been started, and the PI has been actively involved in cleaning and organization of different study databases. Following conducting of all blood assays in August 2013, all data should be immediately ready for statistical analyses.

With regard to academic training, the PI has improved his clinical training further by participating in the weekly Masonic Cancer Center seminars at the University of Minnesota along with seminars held in the PI's Food Science and Nutrition department. The PI has fulfilled majority of his doctorate degree program's requirements including preliminary written and oral exams, teaching requirements for three academic semesters, as well as completing required core and supporting courses (cumulative GPA 3.72). The PI plans to start writing doctoral dissertation and preparing manuscripts immediately upon completion of the study samples and data analyses.

KEY RESERCH ACCOMPLISHMENTS

- Recruitment and randomization of all training grant study participants

- Completing the study for 90.0% of target sample size

- Fulfillment of all required core and supporting coursework

- Contributing to recruitment of 1053 subjects, and completing the study for 481 subjects of the parent grant (as of March 26, 2013)

REPORTABLE OUTCOMES

Given the randomized double-blind design of the study, the PI will not be able to break the codes for treatment and control groups until the last participant completes the study. Therefore, manuscripts are not expected to be written until shortly after August 2013 when samples and data analyses for the entire study participants are fully completed. However, the PI intends to write one manuscript describing the design and recruitment or retention details of the parent study by the end of summer 2013.

Monies from this training grant have been assigned for the payments of the PI's academic costs at the University of Minnesota including tuition and health benefits, as well as stipend for living costs.

CONCLUSION

The Green Tea Modulation of Obesity and Breast Cancer Risk study is a randomized clinical trial designed to understand and elucidate the mechanisms by which green tea may decrease breast cancer risk. This study evaluates the effects of green tea consumption with high EGCG concentrations on obesity-related hormones and inflammatory markers associated with breast cancer risk taking into account different COMT genotypes. The findings from this research will contribute enormously to our understanding of the relationships among green tea supplementation, obesity, and

breast cancer risk, and may ultimately lead to dietary recommendations and/or supplementation for breast cancer prevention. This training grant is right on track according to the approved Statement of Work. It is anticipated that the last participant completes the study by the end of July 2013, and samples and data analyses will be entirely done a few months after.

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